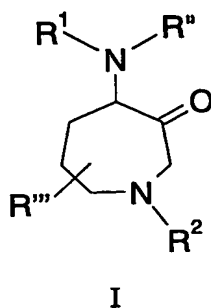


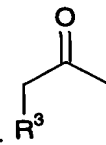
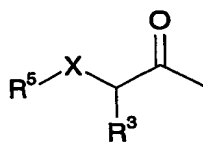
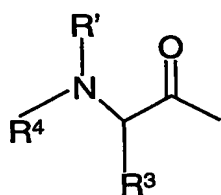
What is claimed is:

1. A method for treating a disease by inhibiting cathepsin S comprising administering at least one compound of Formula I neat or in a pharmaceutically acceptable formulation in an effective amount to a mammal in need thereof, wherein Formula I comprises:



wherein:

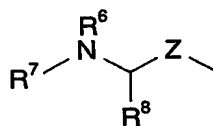
R¹ is



R² is H, C₁₋₆alkyl, C₃₋₆cycloalkyl-C₀₋₆alkyl, Ar-C₀₋₆alkyl, Het-C₀₋₆alkyl, R⁹C(O)-, R⁹C(S)-, R⁹SO₂-, R⁹OC(O)-,

R⁹R¹¹NC(O)-, R⁹R¹¹NC(S)-, R⁹(R¹¹)NSO₂-

of



R³ is H or substituted or unsubstituted C₁₋₆alkyl, C₃₋₇cycloalkylC₀₋₆alkyl, C₄₋₇cycloalkenylC₀₋₆alkyl, C₅₋₈bicycloalkylC₀₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, HetC₀₋₆alkyl, ArC₀₋₆alkyl, Ar-ArC₀₋₆alkyl, Ar-HetC₀₋₆alkyl, Het-ArC₀₋₆alkyl, or Het-HetC₀₋₆alkyl;

R⁴ is H, C₁₋₆alkyl, C₃₋₆cycloalkyl-C₀₋₆alkyl, Ar-C₀₋₆alkyl, Het-C₀₋₆alkyl, R⁵C(O)-, R⁵C(S)-, R⁵SO₂-, R⁵NSO₂-, R⁵OC(O)-, R⁵R¹²NC(O)-, or R⁵R¹²NC(S)-;

R^5 is H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-6} cycloalkyl- C_{0-6} alkyl, Ar- C_{0-6} alkyl, Ar- C_{0-6} alkyl, Ar-Het- C_{0-6} alkyl, Het-Ar- C_{0-6} alkyl, Het-Het- C_{0-6} alkyl, or Het- C_{0-6} alkyl;

R^6 is H, C_{1-6} alkyl, C_{3-6} cycloalkyl- C_{0-6} alkyl, Ar- C_{0-6} alkyl, or Het- C_{0-6} alkyl;

R^7 is H, C_{1-6} alkyl, C_{3-6} cycloalkyl- C_{0-6} alkyl, Ar- C_{0-6} alkyl, Het- C_{0-6} alkyl,

5 $R^{10}C(O)-$, $R^{10}C(S)-$, $R^{10}SO_2-$, $R^{10}OC(O)-$, $R^{10}R^{13}NC(O)-$, or $R^{10}R^{13}NC(S)-$;

R^8 is H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, Het- C_{0-6} alkyl or Ar- C_{0-6} alkyl;

R^9 is C_{1-6} alkyl, C_{3-6} cycloalkyl- C_{0-6} alkyl, Ar- C_{0-6} alkyl or Het- C_{0-6} alkyl;

R^{10} is C_{1-6} alkyl, C_{3-6} cycloalkyl- C_{0-6} alkyl, Ar- C_{0-6} alkyl or Het- C_{0-6} alkyl;

R^{11} is H, C_{1-6} alkyl, Ar- C_{0-6} alkyl, or Het- C_{0-6} alkyl;

10 R^{12} is H, C_{1-6} alkyl, Ar- C_{0-6} alkyl, or Het- C_{0-6} alkyl;

R^{13} is H, C_{1-6} alkyl, Ar- C_{0-6} alkyl, or Het- C_{0-6} alkyl;

R' is H, C_{1-6} alkyl, Ar- C_{0-6} alkyl, or Het- C_{0-6} alkyl;

R'' is H, C_{1-6} alkyl, Ar- C_{0-6} alkyl, or Het- C_{0-6} alkyl;

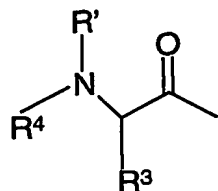
R''' is C_{1-6} alkyl, C_{3-6} cycloalkyl- C_{0-6} alkyl, Ar- C_{0-6} alkyl, or Het- C_{0-6} alkyl;

15 X is CH_2 , S, or O;

Z is $C(O)$ or CH_2 ; or

a pharmaceutically acceptable salt, hydrate or solvate thereof.

2. The method of claim 1 wherein, in Formula:



20 R^1 is (a);

R^2 is R^9SO_2 , $R^9OC(O)-$, or $R^9C(O)-$;

R^3 is C_{5-7} cycloalkyl- C_{1-2} alkyl, C_{4-5} cycloalkenyl- C_{1-2} alkyl, C_{5-8} bicycloalkyl- C_{1-2} alkyl or Ar-Het- C_{0-6} alkyl;

R^4 is $R^5C(O)-$, or R^5SO_2- ;

25 R^5 is unsubstituted or substituted furanyl, tetrahydrofuranyl, morpholinyl, pyrrolyl, piperazinyl, pyrazolyl, isoxazolyl, thiazolyl, pyrazolyl, pyrazolo[5,1-c]pyrimidinyl, triazolyl, pyrazinyl, imadazolyl, benzofuranyl, thiophenyl, furo[3,2-b]-pyridine-2-yl, phenyl, pyridinyl, thieno[3,2-b]thiophenyl, or unsubstituted or C_{1-2} alkylsubstituted pyrazolo[5,1-c]triazinyl;

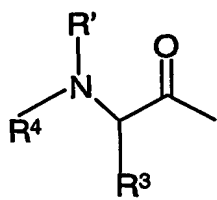
R^9 is Het- C_{0-6} alkyl, Ar- C_{0-6} alkyl, or C_{1-6} alkyl;

30 R' is H, C_{1-6} alkyl;

R'' is H or C_{1-6} alkyl; and

R''' is C₁₋₆alkyl.

3. The method of claim 1 or 2 wherein in Formula I,



R¹ is

R² is R⁹SO₂ R⁹OC(O)-, or R⁹C(O)-;

R³ is cyclopentylmethyl, cyclopentylethyl, cyclopentenylmethyl, cyclopentenylethyl, cyclohexylmethyl, 4-methylcyclohexylmethyl, 2-cyclohexylprop-1-yl, cyclohexylethyl, cycloheptylmethyl, 7,7-dimethylbicyclo[2.2.1]hept-1ylmethyl, or indol-2-ylmethyl;

R⁴ is R⁵C(O)- or R⁵SO₂-

R⁵ is furan-2-yl, furan-3-yl, 2-methylfuran-3-yl, 2,4-dimethylfuran-3-yl, 5-phenylfuran-2-yl, 5-(2-chlorophenyl)furan-2-yl, 5-(3-chlorophenyl)furan-2-yl, 5-(4-chlorophenyl)furan-2-yl, 5-(4-fluorophenyl)furan-2-yl, 5-(4-hydroxyphenyl)furan-2-yl, 5-(3-trifluoromethylphenyl)furan-2-yl, 5-(4-trifluoromethylphenyl)furan-2-yl, 5-(3-trifluoromethylphenyl)furan-2-yl, 5-(4-methylphenyl)furan-2-yl, 5-(4-acetylphenyl)furan-2-yl, or 5-trifluoromethylfuran-2-yl;

tetrahydrofuran-2-yl or tetrahydrofuran-3-yl

N-morpholinyl;

pyrrol-2-yl;

piperzin-1-yl or 4-methylpeperzin-1-yl;

1H-pyrazol-2-yl, 1H-pyrazol-4-yl, 1-methyl-2H-pyrazol-2-yl, 2-methyl-2H-pyrazol-2-yl, 1-methyl-2H-pyrazol-3-yl or 2-methyl-2H-pyrazol-3-yl;

isoxazol-5-yl, 3-methylisoxazol-4-yl, 5-methylisoxazol-3-yl, 5-methylisoxazol-4-yl, or 3,5-dimethylisoxazol-4-yl;

thiazol-2-yl, 2-methylthiazol-2-yl, 2,4-dimethylthiazol-5-yl, 2-(2,3-dihydrobenzo[1,4]dioxin-2-yl)thiazol-4-yl, or 4-methyl-2-phenylthiazol-5-yl;

4,7-dimethylpyrazolo[5,1-c]triazin-3-yl;

2-methyl-2H-pyrazol-2-yl;

2,7-dimethylpyrazol[5,1-c]pyrimidin-6-yl;

3-phenyl-3H-{1,2,3}triazol-3-yl;

pyrazin-2-yl or 5-methylpyrazin-2-yl;

1-H-imidazol-2-yl, 1-methyl-1H-imidazol-4-yl or 1-methyl-1H-imidazol-2-yl;

benzofuran-2-yl, 5,6-dimethoxybenzofuran-2-yl, or 5-(2-morpholin-4-yl-ethoxy)benzofuran-2-yl;

thiophene-3-yl, or thiophen-2-yl, 5-pyridin-2-ylthiophen-2-yl, 5-methylthiophenyl 3-methylthiophen-2-yl; or 3-ethoxythiophen-2-yl;

5 furo[3,2-b]pyridine-2-yl or 3-methylfuro[3,2-b]pyridin-2-yl;

phenyl, 4-methylphenyl, 3-chlorophenyl, 4-chlorophenyl, 3-trifluoromethylphenyl, 4-trifluoromethylphenyl, 2-chlorophenyl, 4-fluorophenyl, 4-hydroxyphenyl, or 4-acetylphenyl; pyridin-2-yl; or

thieno[3,2-b]thiophen-2-yl or 5-isoxazol-3-ylthiophen-2-yl;

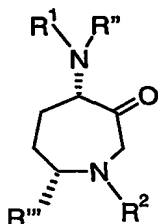
10 R^9 is pyridin-2-yl, 1-oxypyridin-2-yl, phenyl, furan-2-yl or methyl;

R' is H;

R'' is H or C_{1-6} alkyl; and

R''' is methyl.

15 4. The method according to any one of claims 1 - 3 wherein Formula I has the structure:



20 and groups $R^1 - R^{13}$, X, Z, R' , R'' and R''' are the same as defined in any one of claims 1 - 4.

5. The method according to claim 1 wherein the compound of Formula I is morpholine 4-carboxylic acid {(S)-2-[1-methylcyclopentyl-1-(4S,7R)-7-methyl-3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

25 morpholine 4-carboxylic acid {(L)-2-[1-methylcyclopentyl-1-(4S,7R)-7-methyl-3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

morpholine 4-carboxylic acid {(S)-2-[1-methylcyclohexyl-1-(4S,7R)-7-methyl-3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

30 morpholine 4-carboxylic acid {(L)-2-[1-methylcyclohexyl-1-(4S,7R)-7-methyl-3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

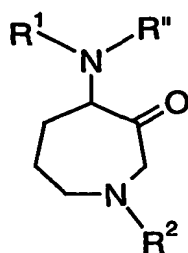
- furan-carboxylic acid {(S)-2-[1-methylcyclohexyl-1-(4S,7R)-7-methyl-3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
- furan-carboxylic acid {(L)-2-[1-methylcyclohexyl-1-(4S,7R)-7-methyl-3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
- 5 furan-carboxylic acid {(S)-2-[4-methylcyclohexyl-1-(4S,7R)-7-methyl-3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
- furan-carboxylic acid {(S)-2-[homocyclopentyl-1-(4S,7R)-7-methyl-3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
- morpholine 4-carboxylic acid {(S)-2-[homocyclopentyl-1-(4S,7R)-7-methyl-3-oxo-1-
- 10 (1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
- furan-carboxylic acid {(S)-2-[cycloheptyl-1-(4S,7R)-7-methyl-3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
- morpholine 4-carboxylic acid {(S)-2-[cycloheptyl-1-(4S,7R)-7-methyl-3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
- 15 furan-carboxylic acid {(S)-2-[cyclopentenyl-1-(4S,7R)-7-methyl-3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
- furan-carboxylic acid {(S)-2-[tryptophanyl-1-(4S,7R)-7-methyl-3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
- morpholine 4-carboxylic acid {(S)-2-(7,7-dimethyl-bicyclo[2.2.1]hepty-1-yl)-1-
- 20 [(4S,7R)-7-methyl-3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
- 2-methyl-2H-pyrazole-3-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
- 1H-pyrazole-2-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
- 25 1-methyl-1H-pyrrole-2-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
- isoxazole-5-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
- thiazole-2-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-
- 30 2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
- 5-trifluoromethyl-furan-2-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
- 1H-pyrazole-4-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

- tetrahydrofuran-3-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
- 4,7-dimethyl-pyrazolo[5,1-c][1,2,4]triazine-3-carboxylic acid {(S)-2-cyclopentyl-1-[(4S,7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
- 5 2,7-dimethyl-pyrazolo[5,1-a]pyrimidine-6-carboxylic acid {(S)-2-cyclopentyl-1-[(4S,7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
- 3-phenyl-3H-[1,2,3]triazole-4-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
- 2-(2,3-dihydro-benzo[1,4]dioxin-2-yl)-thiazole-4-carboxylic acid {(S)-2-cyclopentyl-1-[(4S,7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide
- 10 N-[(S)-2-cyclopentyl-1-[(4S,7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl]-2-pyrazol-1-yl-benzamide;
- 4-methyl-2-phenyl-thiazole-5-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
- 15 5-(4-chloro-phenyl)-furan-2-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
- 5-(3-trifluoromethyl-phenyl)-furan-2-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
- 5-(2-chloro-phenyl)-furan-2-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
- 20 5-(4-fluoro-phenyl)-furan-2-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
- 5-(4-methoxy-phenyl)-furan-2-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
- 25 5-phenyl-furan-2-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
- 5-(4-trifluoromethyl-phenyl)-furan-2-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
- 5-(3-chloro-phenyl)-furan-2-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
- 30 5-(4-methylphenyl)furan-2-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
- 5-(4-acetyl-phenyl)-furan-2-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

- 4-methyl-piperazine-1-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
- piperazine-1-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
- 5 morpholine 4-carboxylic acid {(S)-2-[1-methylcyclohexyl-1-(4S,7R)-7-methyl-3-oxo-1-(1-pyridin-2-yl-meyhanoyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
- morpholine 4-carboxylic acid {(L)-2-[1-methylcyclohexyl-1-(4S,7R)-7-methyl-3-oxo-1-(1-pyridin-2-yl-methanoyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
- 2-methyl-thiazole-4-carboxylic acid {(S)-2-[1-methylcyclohexyl-1-(4S,7R)-7-methyl-3-oxo-1-(1-pyridin-2-yl-meyhanoyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
- 10 3-oxo-1-(1-pyridin-2-yl-meyhanoyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
- 2-methyl-thiazole-4-carboxylic acid {(L)-2-[1-methylcyclohexyl-1-(4S,7R)-7-methyl-3-oxo-1-(1-pyridin-2-yl-methanoyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
- morpholine 4-carboxylic acid {(S)-2-[1-methylcyclohexyl-1-(4S,7R)-7-methyl-3-oxo-1-(1-pyridin-2-yl-meyhanoyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
- 15 morpholine 4-carboxylic acid {(L)-2-[1-methylcyclohexyl-1-(4S,7R)-7-methyl-3-oxo-1-(1-pyridin-2-yl-methanoyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
- 2-methyl-thiazole-4-carboxylic acid {(S)-2-[1-methylcyclohexyl-1-(4S,7R)-7-methyl-3-oxo-1-(1-pyridin-2-yl-meyhanoyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
- 2-methyl-thiazole-4-carboxylic acid {(L)-2-[1-methylcyclohexyl-1-(4S,7R)-7-methyl-3-oxo-1-(1-pyridin-2-yl-methanoyl)-azepan-4-ylcarbamoyl]-ethyl}-amide; or a
- 20 pharmaceutically acceptable salt, hydrate or solvate thereof.

6. The method of claim 1 wherein the inhibition of cathepsin S effects treatment or prevention of an autoimmune disease; treatment or prevention of a disease caused by the formation of atherosclerotic lesions and complications arising therefrom; and diseases requiring inhibition, for therapy, of a class II MHC-restricted immune response, inhibition of an asthmatic response, inhibition of an allergic response, inhibition of immune response against a transplanted organ or tissue, or inhibition of elastase activity in atheroma.

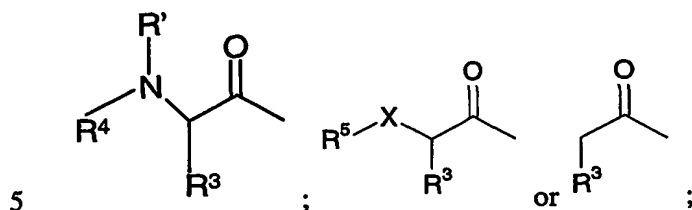
30 7. A compound of Formula II



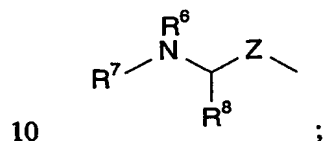
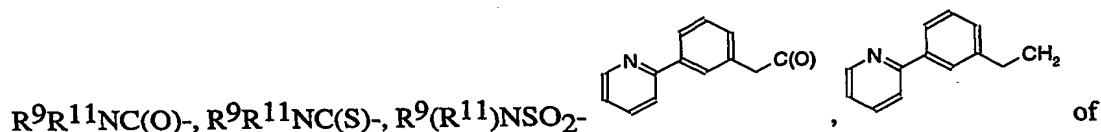
II

wherein:

R¹ is:



R² is H, C₁₋₆alkyl, C₃₋₆cycloalkyl-C₀₋₆alkyl, Ar-C₀₋₆alkyl, Het-C₀₋₆alkyl, R⁹C(O)-, R⁹C(S)-, R⁹SO₂-, R⁹OC(O)-,



R³ is H or substituted or unsubstituted C₁₋₆alkyl, C₃₋₇cycloalkylC₀₋₆alkyl, C₄₋₇cycloalkenylC₀₋₆alkyl, C₅₋₈bicycloalkylC₀₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, HetC₀₋₆alkyl, ArC₀₋₆alkyl, Ar-ArC₀₋₆alkyl, Ar-HetC₀₋₆alkyl, Het-ArC₀₋₆alkyl, or Het-HetC₀₋₆alkyl;

15 R⁴ is H, C₁₋₆alkyl, C₃₋₆cycloalkyl-C₀₋₆alkyl, Ar-C₀₋₆alkyl, Het-C₀₋₆alkyl, R⁵C(O)-, R⁵C(S)-, R⁵SO₂-, R⁵NSO₂-, R⁵OC(O)-, R⁵R¹²NC(O)-, or R⁵R¹²NC(S)-;

R⁵ is H, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₆cycloalkyl-C₀₋₆alkyl, Ar-C₀₋₆alkyl, Ar-ArC₀₋₆alkyl, Ar-HetC₀₋₆alkyl, Het-ArC₀₋₆alkyl, Het-HetC₀₋₆alkyl, or Het-C₀₋₆alkyl;

R⁶ is H, C₁₋₆alkyl, C₃₋₆cycloalkyl-C₀₋₆alkyl, Ar-C₀₋₆alkyl, or Het-C₀₋₆alkyl;

20 R⁷ is H, C₁₋₆alkyl, C₃₋₆cycloalkyl-C₀₋₆alkyl, Ar-C₀₋₆alkyl, Het-C₀₋₆alkyl, R¹⁰C(O)-, R¹⁰C(S)-, R¹⁰SO₂-, R¹⁰OC(O)-, R¹⁰R¹³NC(O)-, or R¹⁰R¹³NC(S)-;

R⁸ is H, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, HetC₀₋₆alkyl or ArC₀₋₆alkyl;

R^9 is C_{1-6} alkyl, C_{3-6} cycloalkyl- C_{0-6} alkyl, Ar- C_{0-6} alkyl or Het- C_{0-6} alkyl;

R^{10} is C_{1-6} alkyl, C_{3-6} cycloalkyl- C_{0-6} alkyl, Ar- C_{0-6} alkyl or Het- C_{0-6} alkyl;

R^{11} is H, C_{1-6} alkyl, Ar- C_{0-6} alkyl, or Het- C_{0-6} alkyl;

R^{12} is H, C_{1-6} alkyl, Ar- C_{0-6} alkyl, or Het- C_{0-6} alkyl;

5 R^{13} is H, C_{1-6} alkyl, Ar- C_{0-6} alkyl, or Het- C_{0-6} alkyl;

R' is H, C_{1-6} alkyl, Ar- C_{0-6} alkyl, or Het- C_{0-6} alkyl;

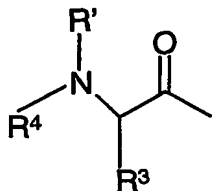
R'' is C_{1-6} alkyl, Ar- C_{0-6} alkyl, or Het- C_{0-6} alkyl;

X is CH_2 , S, or O;

Z is C(O) or CH_2 ; or

10 a pharmaceutically acceptable salt, hydrate or solvate thereof.

8. A compound of Formula I according to claim 7 wherein:



R^1 is (a);

R^2 is R^9SO_2 , $R^9OC(O)-$, $R^9C(O)-$ or C_{1-6} alkyl;

15 R^3 is C_{5-7} cycloalkyl C_{1-2} alkyl, C_{4-5} cycloalkenyl C_{1-2} alkyl, C_{5-8} bicycloalkyl C_{1-2} alkyl or Ar-Het C_{0-6} alkyl;

R^4 is $R^5C(O)-$, or R^5SO_2- ;

R^5 is unsubstituted or substituted furanyl, tetrahydrofuranyl, morpholinyl, pyrrolyl, piperazinyl, pyrazolyl, isoxazolyl, thiazolyl, pyrazolyl, pyrazolo[5,1-c]pyrimidinyl, triazolyl, pyrazinyl, imadazolyl, benzofuranyl, thiophenyl, furo[3,2-b]-pyridine-2-yl, phenyl, pyridinyl, thieno[3,2-b]thiophenyl, or unsubstituted or C_{1-2} alkylsubstituted pyrazolo[5,1-c]triazinyl;

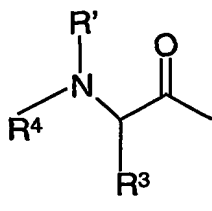
R^9 is Het- C_{0-6} alkyl, Ar C_{0-6} alkyl or C_{1-6} alkyl;

R' is H, C_{1-6} alkyl; and

R'' is H or C_{1-6} alkyl.

25

9 A compound of Formula II according to claim 8 wherein:



R^1 is (a)

R^2 is R^9SO_2 , $R^9OC(O)-$, or $R^9C(O)-$;

R³ is cyclopentylmethyl, cyclopentylethyl, cyclopentenylmethyl, cyclopentenylethyl, cyclohexylmethyl, 4-methylcyclohexylmethyl, 2-cyclohexylprop-1-yl, cyclohexylethyl, cycloheptylmethyl, 7,7-dimethylbicyclo[2.2.1]hept-1-ylmethyl, or indol-2-ylmethyl;

R⁴ is R⁵C(O)- or R⁵SO₂-

- 5 R⁵ is furan-2-yl, furan-3-yl, 2-methylfuran-3-yl, 2,4-dimethylfuran-3-yl, 5-phenylfuran-2-yl, 5-(2-chlorophenyl)furan-2-yl, 5-(3-chlorophenyl)furan-2-yl, 5-(4-chlorophenyl)furan-2-yl, 5-(4-fluorophenyl)furan-2-yl, 5-(4-hydroxyphenyl)furan-2-yl, 5-(3-trifluoromethylphenyl)furan-2-yl, 5-(4-trifluoromethylphenyl)furan-2-yl, 5-(3-trifluoromethylphenyl)furan-2-yl, 5-(4-methylphenyl)furan-2-yl, 5-(4-acetylphenyl)furan-2-yl,
- 10 or 5-trifluoromethylfuran-2-yl;
- tetrahydrofuran-2-yl or tetrahydrofuran-3-yl
- N-morpholinyl;
- pyrrol-2-yl;
- piperzin-1-yl or 4-methylpiperzin-1-yl;
- 15 1H-pyrazol-2-yl, 1H-pyrazol-4-yl, 1-methyl-2H-pyrazol-2-yl, 2-methyl-2H-pyrazol-2-yl, 1-methyl-2H-pyrazol-3-yl or 2-methyl-2H-pyrazol-3-yl;
- isoxazol-5-yl, 3-methylisoxazol-4-yl, 5-methylisoxazol-3-yl, 5-methylisoxazol-4-yl, or 3,5-dimethylisoxazol-4-yl;
- thiazol-2-yl, 2-methylthiazol-2-yl, 2,4-dimethylthiazol-5-yl, 2-(2,3-
- 20 dihydrobenzo[1,4]dioxin-2-yl)thiazol-4-yl, or 4-methyl-2-phenylthiazol-5-yl;
- 4,7-dimethylpyrazolo[5,1-c]triazin-3-yl;
- 2-methyl-2H-pyrazol-2-yl;
- 2,7-dimethylpyrazol[5,1-c]pyrimidin-6-yl;
- 3-phenyl-3H-{1,2,3}triazol-3-yl;
- 25 pyrazin-2-yl or 5-methylpyrazin-2-yl;
- 1-H-imidazol-2-yl, 1-methyl-1H-imidazol-4-yl or 1-methyl-1H-imidazol-2-yl;
- benzofuran-2-yl, 5,6-dimethoxybenzofuran-2-yl, or 5-(2-morpholin-4-yl-ethoxy)benzofuran-2-yl;
- thiophene-3-yl, or thiophen-2-yl, 5-pyridin-2-ylthiophen-2-yl, 5-methylthiophenyl 3-
- 30 methylthiophen-2-yl; or 3-ethoxythiophen-2-yl;
- furo[3,2-b]-pyridine-2-yl or 3-methylfuro[3,2-b]pyridin-2-yl;
- phenyl, 4-methylphenyl, 3-chlorophenyl, 4-chlorophenyl, 3-trifluoromethylphenyl, 4-trifluoromethylphenyl, 2-chlorophenyl, 4-fluorophenyl, 4-hydroxyphenyl, or 4-acetylphenyl;
- pyridin-2-yl; or
- 35 thieno[3,2-b]thiophen-2-yl or 5-isoxazol-3-ylthiophen-2-yl;

R⁹ is pyridin-2-yl, phenyl, furan-2-yl or methyl;

R' is H; and

R'' is H or C₁₋₆alkyl.

- 5 10. A compound of Formula II according to any one of claims 7 - 9 wherein:
 - furan-2-carboxylic acid {(S)-2-homocyclohexyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
 - furan-2-carboxylic acid {(S)-2-tryptophanyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
 - 10 5-trifluoromethyl-furan-2-carboxylic acid {(S)-2-cyclohexyl-1-[(s)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
 - 2,4-dimethyl-thiazole-5-carboxylic acid {(S)-2-cyclohexyl-1-[(s)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
 - 5-methyl-pyrazine-2-carboxylic acid {(S)-2-cyclohexyl-1-[(s)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
 - 15 1-methyl-1H-imidazole-2-carboxylic acid {(S)-2-cyclohexyl-1-[(s)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
 - 1H-pyrazole-4-carboxylic acid {(S)-2-cyclohexyl-1-[(s)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
 - 20 4-methyl-2-phenyl-thiazole-5-carboxylic acid {(S)-2-cyclohexyl-1-[(s)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
 - 2,5-dimethyl-furan-3-carboxylic acid {(S)-2-cyclohexyl-1-[(S)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
 - 2-methyl-furan-3-carboxylic acid {(S)-2-cyclohexyl-1-[(S)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
 - 25 isoxazole-5-carboxylic acid {(S)-2-cyclohexyl-1-[(S)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
 - 5-methyl-isoxazole-3-carboxylic acid {(S)-2-cyclohexyl-1-[(S)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
 - 30 5-methyl-isoxazole-4-carboxylic acid {(S)-2-cyclohexyl-1-[(S)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
 - 3-methyl-isoxazole-4-carboxylic acid {(S)-2-cyclohexyl-1-[(S)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
 - 2-methyl-2H-pyrazole-3-carboxylic acid {(S)-2-cyclohexyl-1-[(S)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
 - 35

- pyrazine-2-carboxylic acid {(S)-2-cyclohexyl-1-[(S)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
- thiazole-2-carboxylic acid {(S)-2-cyclohexyl-1-[(S)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
- 5 2-methyl-thiazole-4-carboxylic acid {(S)-2-cyclohexyl-1-[(S)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;
- (S)-3-cyclohexyl-N-[(S)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-2-(thiophene-2-sulfonylamino)-propionamide;
- (S)-3-cyclohexyl-2-(1-methyl-1H-imidazole-4-sulfonylamino)-N-[(S)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-propionamide;
- 10 (S)-3-cyclohexyl-2-(3,5-dimethyl-isoxazole-4-sulfonylamino)-N-[(S)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-propionamide;
- (S)-3-cyclohexyl-2-(furan-2-sulfonylamino)-N-[(S)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-propionamide;
- 15 (S)-3-cyclohexyl-N-[(S)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-2-(pyridine-2-sulfonylamino)-propionamide;
- (S)-3-cyclohexyl-2-(morpholine-4-sulfonylamino)-N-[(S)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-propionamide;
- (S)-3-cyclohexyl-2-(5-isoxazol-3-yl-thiophene-2-sulfonylamino)-N-[(S)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-propionamide;
- 20 4-[(S)-3-cyclopentyl-2-[(1-furan-2-yl-methanoyl)-amino]-propanoylamino]-3-oxo-azepane-1-carboxylic acid benzyl ester;
- furan-2-carboxylic acid {(S)-2-cyclopentyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]ethyl}-amide;
- 25 furan-2-carboxylic acid [(S)-2-cyclopentyl-1-(1-methanesulfonyl-3-oxo-azepan-4-ylcarbamoyl)-ethyl]-amide;
- furan-2-carboxylic acid [(S)-1-(1-benzenesulfonyl-3-oxo-azepan-4-ylcarbamoyl)-2-cyclopentyl-ethyl]-amide
- furan-2-carboxylic acid {(S)-2-cyclopentyl-1-[1-(1-furan-2-yl-methanoyl)-3-oxo-azepan-4-ylcarbamoyl]-ethyl}-amide;
- 30 furan-2-carboxylic acid {(S)-2-cyclopentyl-1-[3-oxo-1-(1-phenyl-methanoyl)-azepan-4-ylcarbamoyl]-ethyl}-amide; or
- piperazine-1-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide; or
- 35 a pharmaceutically acceptable salt, hydrate or solvate thereof.